



# Diabetes as a Risk Factor for Poor Early Outcomes in Patients Hospitalized With COVID-19

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## OBJECTIVE

Diabetes and obesity are highly prevalent among hospitalized patients with coronavirus disease 2019 (COVID-19), but little is known about their contributions to early COVID-19 outcomes. We tested the hypothesis that diabetes is a risk factor for poor early outcomes, after adjustment for obesity, among a cohort of patients hospitalized with COVID-19.

## RESEARCH DESIGN AND METHODS

We used data from the Massachusetts General Hospital (MGH) COVID-19 Data Registry of patients hospitalized with COVID-19 between 11 March 2020 and 30 April 2020. Primary outcomes were admission to the intensive care unit (ICU), need for mechanical ventilation, and death within 14 days of presentation to care. Logistic regression models were adjusted for demographic characteristics, obesity, and relevant comorbidities.

## RESULTS

Among 450 patients, 178 (39.6%) had diabetes—mostly type 2 diabetes. Among patients with diabetes versus patients without diabetes, a higher proportion was admitted to the ICU (42.1% vs. 29.8%, respectively,  $P = 0.007$ ), required mechanical ventilation (37.1% vs. 23.2%,  $P = 0.001$ ), and died (15.9% vs. 7.9%,  $P = 0.009$ ). In multivariable logistic regression models, diabetes was associated with greater odds of ICU admission (odds ratio 1.59 [95% CI 1.01–2.52]), mechanical ventilation (1.97 [1.21–3.20]), and death (2.02 [1.01–4.03]) at 14 days. Obesity was associated with greater odds of ICU admission (2.16 [1.20–3.88]) and mechanical ventilation (2.13 [1.14–4.00]) but not with death.

## CONCLUSIONS

Among hospitalized patients with COVID-19, diabetes was associated with poor early outcomes, after adjustment for obesity. These findings can help inform patient-centered care decision making for people with diabetes at risk for COVID-19.

Diabetes is one of the most common chronic conditions in the U.S., currently estimated to affect 34.2 million people (10.5% of the U.S. population) (1). In addition to the well-documented adverse health outcomes associated with this disease, diabetes has also emerged as a commonly reported risk factor among people hospitalized with coronavirus disease 2019 (COVID-19), caused by infection with the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (2–7). Following initial reports of COVID-19 in Washington state (January 2020) (8), COVID-19 has spread rapidly and resulted in >3.0 million cases and nearly 135,000 deaths in the U.S. as of

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July 2020 (9). The convergence of these two epidemics has raised critical questions about the relationship between diabetes and COVID-19 severity (10,11), particularly in light of the increasing recognition that obesity, which is also highly prevalent in the U.S., is also a strong risk factor for severe COVID-19 (12–14).

Consistent with early reports emerging from China (15,16), several U.S. studies have confirmed a high prevalence of diabetes and obesity among hospitalized patients with COVID-19 (4,13,17). However, few studies have evaluated whether patients with diabetes who are hospitalized with COVID-19 are more likely to experience poor early outcomes (4,11) and whether this association remains after adjustment for obesity status (4,13). Given that ~61% of people with diabetes in the U.S. have obesity (1), understanding the contribution of these comorbidities to early outcomes among people hospitalized with COVID-19 is critically important to inform patient-centered care decision making for people with these conditions. In this study, we tested the hypothesis that diabetes is associated with poor early outcomes of hospitalization with COVID-19, even after obesity and other relevant clinical characteristics are accounted for.

## RESEARCH DESIGN AND METHODS

### Data Source and Sample

This study used data from the Massachusetts General Hospital (MGH) COVID-19 Data Registry. Patients were eligible for inclusion in the registry if they presented to care (defined as the first contact with the health care system with COVID-19 symptoms) and were subsequently hospitalized at MGH with PCR-confirmed SARS-CoV-2 infection between 11 March 2020 and 30 April 2020. Over the study period, MGH had the highest total number of hospitalized patients with COVID-19 in Massachusetts, which in turn has had one of the largest COVID-19 case numbers in the U.S. as of June 2020 (9,18). All patients included in our study were followed for 14 days from the date of initial presentation to care with COVID-19. General inpatient diabetes at MGH is managed mostly by the primary medical team with basal-bolus supplemental insulin or supplemental insulin alone for mild hyperglycemia, whereas insulin drips are favored in the intensive care unit (ICU) setting. Specialty consultation is widely available for challenging cases.

Additional registry data were collected by performance of manual chart review for key aspects of the past medical history and details of the hospitalization. Chart review was performed by physicians and research nurses and their assistants. All members of the chart review team underwent detailed training on the standard operating procedure for data extraction, which was also subjected to quality checks to ensure data accuracy and minimize missing variables. In addition, height, weight, and BMI as well as hemoglobin A<sub>1c</sub> (HbA<sub>1c</sub>) obtained during the hospitalization and blood glucose at admission during the index hospitalization were obtained electronically through the Enterprise Data Warehouse (EDW), a repository that was derived from the Epic electronic medical records system. For patients with diabetes who did not have an HbA<sub>1c</sub> measured during the index hospitalization, we obtained HbA<sub>1c</sub> values directly from the historical electronic medical record if available within the year preceding the index hospitalization for inclusion in a subgroup analysis of the relationship between baseline glycemic control and 14-day outcomes. The registry and this research were approved by the Partners HealthCare Institutional Review Board (protocol number 2020P000829).

### Definitions of Diabetes, Obesity, and Clinical Covariates

Diabetes was defined based on the following criteria: 1) past medical history of diabetes as documented in the medical record and manually retrieved on chart review, 2) HbA<sub>1c</sub>  $\geq$  6.5% during the index hospitalization, or 3) random blood glucose  $\geq$  200 mg/dL at admission to the hospital with supportive history by chart review. Only four individuals had a presenting random blood glucose of  $\geq$  200 mg/dL in the absence of a recent elevated HbA<sub>1c</sub> or chart review diagnosis of diabetes. Two endocrinologists adjudicated these cases and determined that two of the four individuals had diabetes. The distribution of diabetes diagnoses based on these criteria is provided in the Supplementary Materials (p. 2). BMI, defined as weight in kilograms divided by the square of height in meters, was available from the EDW and was defined using standard BMI thresholds of  $<$  18.5 kg/m<sup>2</sup> for underweight, 18.5–24.9 kg/m<sup>2</sup> for normal weight, 25.0–29.9 kg/m<sup>2</sup> for overweight, and  $\geq$  30.0 kg/m<sup>2</sup> for obese.

Additional analyses with subcategorization of the BMI  $\geq$  30.0 kg/m<sup>2</sup> group into  $\geq$  30.0–34.9 kg/m<sup>2</sup> and  $\geq$  35.0 kg/m<sup>2</sup> are provided in the Supplementary Materials (p. 7). Models were adjusted for race/ethnicity (available from the EDW based on self-report) and defined as non-Hispanic White, non-Hispanic African American, Hispanic, other, and unknown. Finally, we manually extracted comorbidities that have commonly been reported among hospitalized patients with COVID-19 (17): coronary artery disease (CAD) or myocardial infarction (MI), congestive heart failure (CHF) (including both heart failure with preserved ejection fraction and heart failure with reduced ejection fraction), hypertension, renal disease, liver disease, chronic obstructive pulmonary disease (COPD) or asthma, and active malignancy, using standard clinical diagnostic criteria.

### Statistical Analysis

The primary outcomes in this study were 1) admission to the ICU, 2) need for mechanical ventilation, and 3) death among hospitalized patients with COVID-19 within 14 days of presentation to care. These states were not mutually exclusive, so an individual could experience more than one of these outcomes within the 14-day period. The exposure of interest was diabetes as defined above and, as a secondary exposure of interest, BMI category. We first described differences in the demographic and health characteristics by diabetes status. We used *t* tests to compare means and  $\chi^2$  tests to compare proportions. We then stratified the cohort by diabetes status and BMI category and compared the proportions of people with and without diabetes within each BMI category for all three outcomes using  $\chi^2$  tests. To test the hypothesis that poor baseline glycemic control would be associated with severe COVID-19, we conducted a subanalysis of the group with diabetes and compared the proportion of people by outcome according to HbA<sub>1c</sub> values obtained either during the hospitalization if available or using the most recent value available in the year preceding the index hospitalization. HbA<sub>1c</sub> was categorized as poor glycemic control (HbA<sub>1c</sub>  $>$  9.0% according to HEDIS definition [19]) versus better glycemic control:  $\leq$  7.0% and  $>$  7.0–9.0%. Lastly, we conducted univariate and multivariable logistic regression to evaluate the

association of diabetes, BMI category, and each of the primary outcomes. Multivariable models were additionally adjusted for age, sex, race/ethnicity, and comorbidities. Given that there were individuals who died prior to being mechanically ventilated, we conducted sensitivity analyses that excluded these individuals as well as a composite outcome “mechanical ventilation or death,” which we provide in the Supplementary Materials (p.6). In all analyses, results were considered statistically significant if the corresponding *P* value was <0.05. Analyses were conducted in Stata v. 15.1.

## RESULTS

This article reports on 450 people who were eligible for inclusion in the MGH COVID-19 Data Registry and were hospitalized at MGH with SARS-CoV-2 infection between 11 March 2020 and 30 April 2020. The baseline characteristics of the study population are summarized in Table 1. Of the 450 patients, 178 (39.6%) had diabetes, the vast majority of which was type 2 diabetes (mean HbA<sub>1c</sub> 8.1%). Patients with diabetes were older than those without diabetes (mean age 66.7 vs. 61.6 years), and 42.1% of patients with diabetes were age ≥70 years (Table 1). There was a higher proportion of patients with diabetes who had obesity (51.4%,  $\chi^2_{df=2} = 9.6$ , *P* = 0.008) compared with the proportion of those without diabetes (36.8%). A higher proportion of patients with diabetes had a past medical history of CHF, hypertension, and renal disease compared with the proportion of patients without diabetes (Table 1).

### Outcomes by Diabetes, BMI Category, and Baseline Glycemic Control

There were 156 ICU admissions, 129 people who required mechanical ventilation, and 49 deaths during the first 14 days after presentation to care. Among patients with diabetes versus patients without diabetes, a higher proportion was admitted to the ICU (42.1% vs. 29.8%, respectively,  $\chi^2_{df=1} = 7.3$ , *P* = 0.007), had mechanical ventilation (37.1% vs. 23.2%,  $\chi^2_{df=1} = 10.2$ , *P* = 0.001), or died (15.9% vs 7.9%,  $\chi^2_{df=1} = 6.8$ , *P* = 0.009) over this time horizon (Fig. 1). The numerical counts for patients requiring ICU admission and mechanical ventilation were higher for people with diabetes than for people without diabetes within

each BMI category, but pairwise comparisons of the proportions did not achieve statistical significance (Fig. 2). In a sub-analysis of people with diabetes and HbA<sub>1c</sub> (*n* = 168), the proportion of people who required ICU admission and mechanical ventilation was greater among people with HbA<sub>1c</sub> >9.0 (52.5% and 47.5%, respectively) than among people with HbA<sub>1c</sub> >7.0–9.0% (40.3% and 36.1%, respectively) and ≤7.0% (41.4% and 33.9%, respectively), but the differences did not achieve statistical significance at the 0.05 level (Supplementary Materials, p. 3). Multivariable logistic regression models that include baseline glycemic control as a dichotomous variable are provided in the Supplementary Materials (p. 4).

### Logistic Regression Models of ICU Admission, Mechanical Ventilation, and Death

Univariate models are provided in the Supplementary Materials (p. 5). In multivariable logistic regression models, diabetes was associated with greater odds of ICU admission (odds ratio [OR] 1.59 [95% CI 1.01–2.52]), mechanical ventilation (1.97 [1.21–3.20]), and death (2.02 [1.01–4.03]) after adjustment for age-group, sex, race/ethnicity, BMI category, and medical comorbidities (Table 2). Obesity was associated with greater odds of ICU admission (2.16 [1.20–3.88]) and mechanical ventilation (2.13 [1.14–4.00]) but not with greater odds of death (1.10 [0.50–2.45]) (Table 2). Age ≥70 years was associated with increased odds of death (12.66 [1.50–106.56]), after adjustment for all other characteristics. Male sex (1.60 [1.00–2.57]) and Hispanic ethnicity (1.94 [1.08–3.44]) were associated with need for mechanical ventilation as compared with female sex and White/Non-Hispanic race/ethnicity, respectively. Interaction terms for diabetes and obesity in the models of both ICU admission and need for mechanical ventilation were tested and were not statistically significant. In a sensitivity analysis that excluded people who died without having mechanical ventilation, the association between diabetes and mechanical ventilation (OR 2.01 [1.24–3.25]) and obesity and mechanical ventilation (2.01 [1.05–3.82]) remained of a magnitude and significance similar to those in the primary analysis (Supplementary Materials, p. 6). Multivariable logistic regression analysis with additional subcategorization of the BMI group ≥30.0 kg/m<sup>2</sup>

showed that BMI ≥30.0–34.9 kg/m<sup>2</sup> remained associated with greater odds of ICU admission (2.20 [1.14–4.27]) and mechanical ventilation (2.32 [1.15–4.68]), but the ≥35.0 kg/m<sup>2</sup> category was only associated with greater odds of ICU admission (2.11 [1.09–4.09]) (Supplementary Materials, p. 7).

## CONCLUSIONS

In this observational study of 450 patients hospitalized with COVID-19, we found that compared with proportions of patients without diabetes, greater proportions of patients with diabetes were admitted to the ICU, required mechanical ventilation, and died within 14 days of presentation to care. We also found that diabetes was associated with 1.6-fold increased odds of ICU admission, 2.0-fold increased odds of mechanical ventilation, and 2.0-fold increased odds of death within 14 days from presentation to care, after adjustment for obesity. These findings add to the growing body of literature about the relationship of diabetes, obesity, and COVID-19 severity among people hospitalized with COVID-19 in the U.S. and expand our current understanding of the contributions of these two conditions to early outcomes among people hospitalized with COVID-19. Given the high prevalence of diabetes and obesity in the U.S. (1) and the rapidly rising case numbers of COVID-19 (9), these findings have important implications for patient-centered care decision making for people with metabolic disease and COVID-19.

Several other important findings emerged from our analysis. First, we found that the proportion of people with and without diabetes who were admitted to the ICU and who required mechanical ventilation was higher in magnitude with increasing BMI category. We also found that obesity was associated with 2.2-fold increased odds of ICU admission and 2.1-fold increased odds of mechanical ventilation compared with normal weight, after adjustment for diabetes, age, sex, race/ethnicity, and major comorbidities. These findings are consistent with numerous studies reporting that obesity is a strong risk factor for severe COVID-19 (12–14) and add to the current literature by showing that this association persists at lower BMI thresholds than previously reported in a U.S. population (4,13).

Second, we did not find a significant difference in the association between

**Table 1—Characteristics of 450 hospitalized people with COVID-19 and with or without diabetes**

	No diabetes (N = 272)	Diabetes (N = 178)	P
Age (years), mean ± SD	61.1 ± 18.8	66.7 ± 14.2	0.007
Age (years), n (%)			
<50	84 (31)	20 (11.2)	<0.001
50–59	41 (15.1)	41 (23.0)	
60–69	40 (14.8)	42 (23.6)	
≥70	106 (39.1)	75 (42.1)	
Sex, n (%)			
Male	149 (54.8)	110 (61.8)	0.14
Female	123 (45.2)	68 (38.2)	
HbA <sub>1c</sub> (%), mean ± SD	—	8.1 ± 2.0	
Race/ethnicity, n (%)			
White	136 (50.8)	89 (50.3)	0.26
Hispanic	83 (30.5)	41 (23.0)	
African American	18 (6.6)	19 (10.7)	
Other	8 (2.9)	7 (3.9)	
Unknown/missing	27 (9.9)	22 (12.4)	
BMI category, n (%)			
Underweight/normal	67 (24.6)	36 (20.3)	0.008
Overweight	105 (38.3)	50 (28.3)	
Obese	100 (36.8)	91 (51.4)	
Comorbidities, n (%)			
CAD or MI	47 (17.3)	44 (24.7)	0.06
CHF	23 (8.4)	29 (16.3)	0.01
Hypertension	44 (24.7)	134 (75.3)	<0.001
COPD/asthma	66 (24.3)	46 (25.8)	0.71
Cancer (active)	17 (6.3)	4 (2.3)	0.05
Liver disease	25 (9.4)	21 (11.9)	0.41
Renal disease	40 (14.9)	46 (26.0)	0.004

t tests were used to compare means and  $\chi^2$  tests were used to compare proportions. BMI categorization: <18.5 kg/m<sup>2</sup> for underweight, >18.5–24.9 kg/m<sup>2</sup> for normal weight, >25.0–29.9 kg/m<sup>2</sup> for overweight, and >30.0 kg/m<sup>2</sup> for obese. The majority of diabetes cases were type 2 diabetes; only two patients in the cohort had type 1 diabetes.

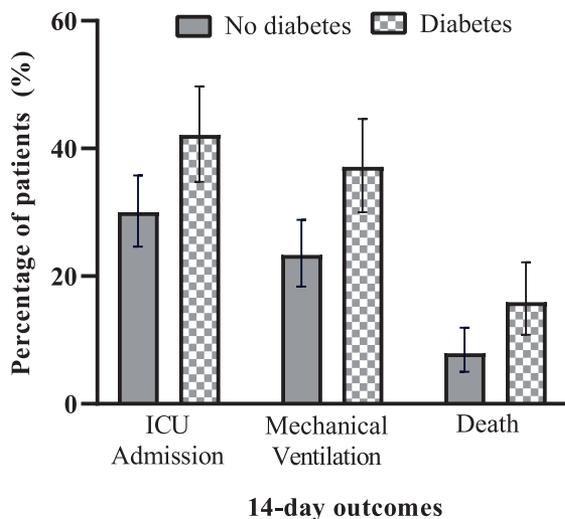
poor baseline glycemic control, as measured by HbA<sub>1c</sub> >9.0 at hospitalization or within the year prior to admission, and early outcomes in this cohort; however, the proportion of patients with severe COVID-19 was higher in magnitude among patients with poor glycemic control compared with that among patients with better glycemic control. Although there has been little study of prehospitalization HbA<sub>1c</sub> and COVID-19 outcomes, mounting evidence suggests that poor glycemic control among hospitalized patients with COVID-19 is associated with adverse outcomes, including higher mortality (20–23). Since the lack of an association between baseline glycemic control and early outcomes may have been limited by sample size in our study, the question of whether baseline glycemic control is associated with poor early COVID-19 outcomes remains a critically important one in consideration of the implications for risk stratification for this patient population.

Third, we found that Hispanic ethnicity was associated with greater odds of mechanical ventilation. This finding is consistent with recent data showing that ethnic minorities in the U.S. have a greater risk of poor COVID-19 outcomes (24–27). However, understanding the relationship between race/ethnicity and COVID-19 severity requires a more complex framework than afforded by the scope of this analysis. Given the limited data on racial/ethnic disparities and COVID-19 severity, future studies are needed to better understand these findings. Finally, the lack of an association between other major comorbidities and COVID-19 severity is also consistent with most U.S.-based adjusted analyses to date (4,13) but may also be related to limited power, since these comorbidities were less common than diabetes and obesity in our sample.

Our findings are consistent with numerous studies that have reported a high

prevalence of diabetes among people with severe COVID-19 (2,4,5,7,13,15,28,29) and add to the growing literature regarding the intersection of these epidemics by showing that the relationship between diabetes and increased odds of three key measures of COVID-19 severity at 14 days remains after adjustment for obesity. While several international studies have analyzed the association between diabetes and severe COVID-19 (30,31), only a few studies have presented this association according to stratified outcomes among patients hospitalized with COVID-19 (32,33). In their cross-sectional analysis of 51,633 Mexican subjects with COVID-19, Bello-Chavolla et al. (30) showed that diabetes (self-reported in 18.3% of subjects) and obesity (self-reported in 20.7% of subjects) were associated with greater odds of hospitalization, ICU admission, and mechanical ventilation. With use of a mechanistic COVID-19 lethality score, early-onset diabetes (defined as diabetes among individuals younger than 40 years of age) also emerged as an important predictor of mortality (hazard ratio 2.86 [95% CI 2.19–3.76]). In a similar study of 50,411 Mexican individuals with COVID-19, Gutierrez and Bertozzi reported that diabetes was associated with a 1.21 odds of mechanical ventilation and 1.95 odds of death (32). Although the effect size of these associations was larger in our study, it is possible that the risk was underestimated in the study by Gutierrez and Bertozzi due to use of self-reported diabetes diagnosis only and the possible misclassification of individuals without diabetes who in fact had diabetes.

Few studies evaluating the association between diabetes and COVID-19 severity have been published to date in a U.S. population. In a longitudinal cohort study of 2,729 patients hospitalized with COVID-19 in New York, Petrilli et al. (4) showed that diabetes and obesity (≥40 kg/m<sup>2</sup>) were associated with 1.2 and 1.5 increased odds of critical illness, respectively. However, Petrilli et al. defined critical illness as a composite of care in the ICU, use of mechanical ventilation, discharge to hospice, or death, thus capturing a composite outcome. While composite outcomes are based in an assumption that components have the same directional relationship with the treatment or exposure, our analysis suggests that components of this outcome may have different relationships with



	No diabetes		Diabetes	
	n (%)	95% CI	n (%)	95% CI
ICU Admission	81 (29.8)	24.4-35.6	75 (42.1)	34.8-49.7
Mechanical Ventilation	63 (23.2)	18.3-28.6	66 (37.1)	30.0-44.6
Death	22 (8.2)	5.2-12.2	28 (15.9)	10.8-22.2

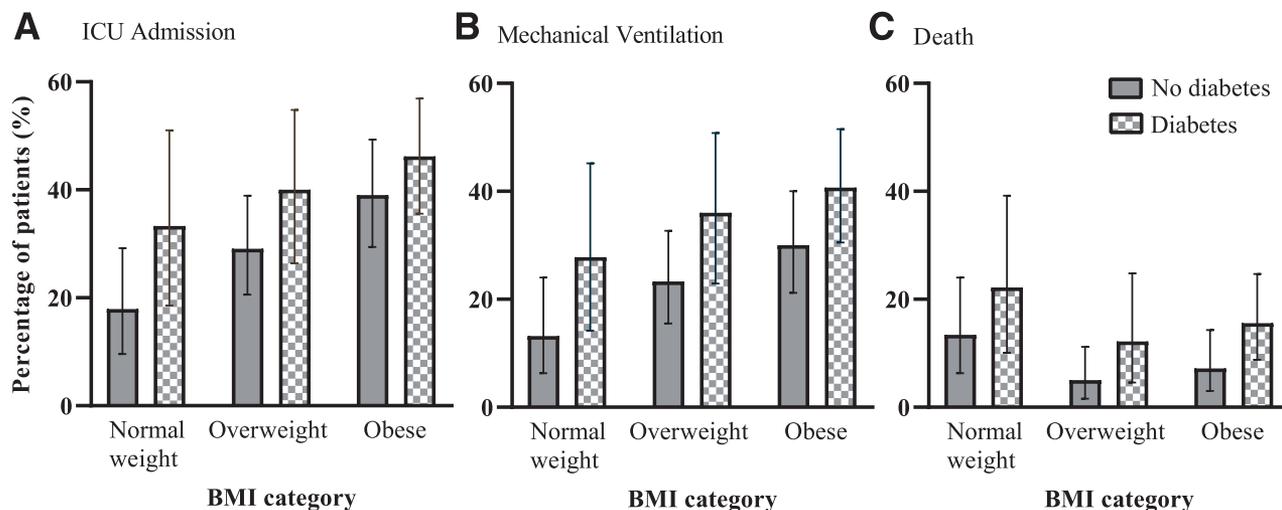
**Figure 1**—Fourteen-day outcomes among 450 hospitalized patients with COVID-19, according to diabetes status. Three outcomes are shown on the x-axis, and the percentage of patients in each outcome group is shown on the y-axis. Within each outcome, all pairwise  $\chi^2$  tests were  $P < 0.05$ .

Aside from previously studied mechanisms that predispose people with diabetes to higher risk of infections, such as impaired immunity (33,34), several mechanisms have been proposed suggesting a specific association between diabetes and SARS-CoV-2 illness severity (2). Rao, Lau, and So (35) showed that diabetes and related traits are associated with increased expression of ACE2, the receptor for SARS-CoV-2, which could influence susceptibility and severity of infection. In addition, cytokines may be another mechanistic link between diabetes and SARS-CoV-2 illness severity. For instance, interleukin-6 (IL-6), a pleiotropic cytokine that is increased in diabetes and metabolic disorders (10), has also emerged as a predictor of poor prognosis among people with COVID-19 (36). However, because most studies are preliminary, additional work is needed to understand mechanisms underlying the association between diabetes and increased COVID-19 severity (7).

One of the strengths of this study is that manual chart review allowed for detailed patient information to be incorporated into the analysis, including the adjudication of diabetes status by endocrinologists. However, this study had several limitations. First, the study was conducted at a single institution in Massachusetts, which had a different COVID-19 prevalence, rate of COVID-19 case increase, and ICU bed capacity (18)

diabetes and obesity. Palaiodimos et al. (13) analyzed data on the first 200 patients admitted with COVID-19 to a tertiary hospital in the Bronx, New York. Patients were followed for 3 weeks after admission to the hospital. In contrast to the findings of our study, only BMI  $\geq 35$

kg/m<sup>2</sup> was associated with poor COVID-19 outcomes (13). Although diabetes did not emerge as a risk factor for severe COVID-19 in their study, the lack of an association may have been due to limitations of a small sample size of people with diabetes ( $n = 79$ ).



**Figure 2**—Fourteen-day outcomes among 450 hospitalized patients with COVID-19, according to diabetes status and BMI category. Each panel represents an outcome: ICU admission (A), mechanical ventilation (B), and death (C). Three BMI categories are shown on the x-axis, and the percentage of patients in each BMI category is shown on the y-axis. Within each BMI category, all pairwise  $\chi^2$  testing was not statistically significant.

**Table 2—Multivariable logistic regression analysis of 14-day outcomes among 450 hospitalized people with COVID-19**

	14-day outcomes, OR (95% CI)		
	ICU admission (N = 436)	Mechanical ventilation (N = 436)	Death (N = 417)
Diabetes	1.59 (1.01–2.52)	1.97 (1.21–3.20)	2.02 (1.01–4.03)
BMI category			
Overweight	1.42 (0.78–2.58)	1.42 (0.75–2.71)	0.60 (0.25–1.44)
Obese	2.16 (1.20–3.88)	2.13 (1.14–4.00)	1.10 (0.50–2.45)
Age (years)			
50–59	1.13 (0.57–2.24)	1.02 (0.50–2.08)	3.74 (0.40–34.54)
60–69	1.22 (0.60–2.49)	1.20 (0.57–2.54)	4.57 (0.50–41.9)
≥70	1.41 (0.69–2.85)	1.72 (0.82–3.61)	12.66 (1.50–106.56)
Male	1.36 (0.88–2.12)	1.60 (1.00–2.57)	1.35 (0.66–2.75)
Race/ethnicity			
Hispanic	1.60 (0.93–2.76)	1.94 (1.08–3.44)	0.44 (0.15–1.25)
African American	1.36 (0.62–2.97)	1.47 (0.64–3.40)	0.35 (0.07–1.62)
Other	2.30 (0.76–6.98)	1.72 (0.53–5.60)	—
Unknown/missing	2.75 (1.38–5.47)	2.34 (1.15–4.76)	0.68 (0.21–2.18)
CAD or MI	0.63 (0.33–1.19)	0.55 (0.27–1.11)	0.71 (0.31–1.61)
CHF	1.65 (0.77–3.51)	0.98 (0.42–2.26)	1.94 (0.78–4.85)
Hypertension	0.96 (0.57–1.60)	0.78 (0.45–1.35)	1.33 (0.57–3.10)
COPD/asthma	0.66 (0.39–1.11)	0.55 (0.31–0.98)	0.75 (0.35–1.60)
Cancer (active)	0.60 (0.18–1.94)	0.55 (0.15–2.05)	1.57 (0.46–5.36)
Liver disease	1.13 (0.57–2.23)	1.10 (0.54–2.25)	0.91 (0.27–3.03)
Renal disease	0.89 (0.49–1.64)	1.09 (0.58–2.09)	1.22 (0.55–2.73)

Reference groups: “no disease” for diabetes and all comorbidities, normal weight for BMI category, age <50 years, female sex, and non-Hispanic White. Events per outcome: 156 people were admitted to the ICU, 129 people were mechanically ventilated, and 49 people died within 14 days of presentation to care.

than the sites of other studies referenced here (4,13). Second, the sample size for this study was limited, which may have affected our ability to detect significant differences, especially in the association between prehospitalization glycemic control and the outcomes of interest. However, despite the small sample size, the completeness of data allowed us to rigorously evaluate the primary exposures, outcomes, and covariates, including medical comorbidities. Another important limitation is that people who died without escalation of care may have opted against admission to the ICU, for instance, due to do-not-resuscitate/do-not-intubate code status, hence reflecting their outcome in the context of their goals of care rather than as part of their course throughout the hospitalization with COVID-19. However, in sensitivity analyses that excluded these individuals and in one that included a composite outcome of mechanical ventilation or death, the magnitude and significance of the main associations reported remained. Lastly, the observational data and methodological approach used in this study identified potentially

important associations but do not establish causal relationships.

The convergence of the diabetes and COVID-19 epidemics has raised critical concerns regarding the heightened illness severity associated with these conditions (10,11). This is a cause for particular concern in the U.S., where the prevalence of metabolic disease is high and may place many people at greater risk of developing severe COVID-19 should they become infected with SARS-CoV-2. In this study, we showed that diabetes was associated with poor early outcomes among hospitalized patients with COVID-19, after adjustment for obesity, which was also a strong risk factor for poor early outcomes. Our findings can help guide risk mitigation efforts and patient-centered care decision making for people with diabetes and obesity, particularly in areas of the U.S. with a high prevalence of diabetes and obesity that are in early phases of the SARS-CoV-2 outbreak. Future research is urgently needed to better understand the mechanisms underlying the relationship between diabetes, obesity, and COVID-19 severity and approaches to

prevent and treat people with metabolic disease and COVID-19.

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**Duality of Interest.** D.J.W. reports serving on a data monitoring committee for Novo Nordisk. A close family member of S.J.C. is employed by a Johnson & Johnson company. J.B.M. is an Academic Associate for Quest Diagnostics. J.H. has consulted for several health care systems. No other potential conflicts of interest relevant to this article were reported.

**Author Contributions.** J.M.-G., J.S., J.P., D.J.W., and J.B.M. co-conceived the study. J.M.-G., J.S., J.P., D.J.W., and J.B.M. led the analysis, which was carried out by J.M.-G. A.S.F. provided additional input on the analysis. J.M.-G., J.S., and J.P. wrote the first draft of the manuscript, and all authors provided critical input on multiple iterations. All authors approved the final version. J.M.-G. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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